

### Remarks

#### 1. Support for Amendments and New Claims

The amendments to claims 1, 11, 17, and 20 are supported by the application as filed. The amendments to claims 1 and 17 are supported throughout the application, for example at page 15 lines 21-22; page 16 lines 1-15; and page 18 lines 19-22. With respect to claims 11 and 20, a cassette wherein each individual microfluidic channel supplies fluid to a single domain is described at page 29, lines 3-9 and in Figures 9 and 10.

Accordingly, the amendments do not add new matter to the application.

#### 2. Claim Rejections – 35 U.S.C. § 103

It is well-established that the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness, before any rejection under § 103 may be made. *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993). Accordingly, “if the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness.” M.P.E.P. § 2142. Citing the Federal Circuit, the M.P.E.P. outlines three basic criteria that must be met to establish a *prima facie* case of obviousness:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant’s disclosure.

M.P.E.P. § 2143 (*citing In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991)).

Moreover, the Patent Office carries the obligation to apply the standard of patentability set forth by the Supreme Court and by the Congress. M.P.E.P. § 2141. Under *Graham v. John*

*Deere*, 383 U.S. 1 (1966), the analysis of obviousness must include an evaluation of the differences between the prior art and the claims at issue. In this context, the question under 35 U.S.C. § 103 is not whether the differences themselves would have been obvious, but rather whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782 (Fed. Cir. 1983). In addition, a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983).

a. Claim 1 is Not *Prima Facie* Obvious

i. The Patent Office Has Not Established a *Prima Facie* Case That  
Previously Pending Claim 1 is Obvious

The Patent Office rejected claims 1 and 9-22 under 35 U.S.C. § 103(a) as unpatentable over Cherukuri et al. (U.S. Pat. 5,980,704) in view of Sanadi et al. (U.S. Pat. 5,741,463).

According to the Examiner, “Cherukuri et al. teach a cassette/fluid array (device tray) including micron-sized reservoirs, connected microchannels (fluid delivery system), and reaction cells etched into a substrate. . . . The reference does not teach a plurality of wells defining the space between the cell binding location and the fluidic location.” Regarding Sanadi et al., the Examiner stated, “Sanadi teaches a cassette that prevents cross-contamination of samples by using a resilient gasket that covers the top of the plate.” Based on these two references, the Examiner concluded, “It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a space defining binding locations and the fluid location as taught by Sanadi with the cassette of Cherukuri et al. because such cassette array devices with

well spacing between the fluid delivery system and binding locations are well known in the art, thereby providing a reasonable expectation of success in utilizing such a configuration.”

With all due respect to the Office, the above argument does not establish a *prima facie* case of obviousness. The first element of the *prima facie* case, a suggestion or motivation to combine the references, is not satisfied since Cherukuri pertains to a microfluidic device while Sanadi pertains to a “multi-well plate which prevents cross-contamination of samples through the use of resilient gasket,” which is a completely unrelated device. Sanadi contains no mention whatsoever of microfluidics; rather, it simply teaches a general-purpose multi-well plate with a gasket. According to the M.P.E.P., “When the motivation to combine the teachings of the references is not immediately apparent, it is the duty of the examiner to explain why the combination of the teachings is proper.” See M.P.E.P. § 2142. did it  
motivate  
statement

The second element of the *prima facie* case, a reasonable expectation of success, is not satisfied either, since by combining Cherukuri with Sanadi one skilled in the art would not arrive at the device of previously pending claim 1. The Examiner stated that the reasonable expectation of success is based on the fact that “cassette array devices with well spacing between the fluid delivery system and binding locations are well known in the art.” However, the combination of Cherukuri and Sanadi fail to teach or suggest cell binding locations, or wells as recited in previously pending claim 1, and thus, even if microfluidic cassette array devices were well known in the art, such devices do not make the applicant’s claimed device obvious under § 103(a). what basis?  
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rejection

Finally, the third element of the *prima facie* case, that every claim limitation must be taught or suggested by the prior art, is not satisfied. As discussed above, the combination of

Cherukuri and Sanadi fail to teach or suggest cell binding locations, or wells as recited in previously pending claim 1.

Based on the above, the Applicants submit that the Patent Office has failed to meet its obligation to establish a prima facie case of obviousness of previously pending claim 1 over the cited references.

ii. The Patent Office Cannot Establish a *Prima Facie* Case That Claim 1, As Amended, is Obvious

As indicated above, the Applicant respectfully traverses the rejection of claim 1 under 35 U.S.C. § 103(a). Nevertheless, in order to advance prosecution, the Applicant has amended claim 1, which now recites:

A cassette for cell screening, comprising

- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites, and wherein a cell binding site comprise a well; and
- (b) a fluid delivery system for delivering a combinatorial of reagents to the wells; wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:
  - (i) a plurality of domains matching the wells on the surface of the base; and
  - (ii) microfluidic channels that supply fluid to the domains.

Thus, amended claim 1 specifically recites that the surface contains a non-uniform micro-patterned chemical array comprising multiple (biological) cell binding sites, and that the cell binding site comprises a well. This clearly is not taught or suggested in the combination of cited references. Cherukuri teaches a device that includes reaction cells (ie: non-biological cells, but merely physical locations). Sanadi fails to cure the deficiency of Cherukuri, since it simply teaches “a multi-well plate which prevents cross-contamination of samples through the use of a resilient gasket.” See Abstract, lines 1-3. Thus, the combination of cited references does not

teach or suggest the limitation that the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites. The combination of references further does not teach or suggest the limitation that a cell binding site (**as recited in the claim**) comprises a well. Furthermore, since the combination of cited references does not teach or suggest these limitations, they necessarily cannot teach or suggest a chamber that comprises a plurality of domains matching the wells (**as recited in the claim**) on the surface of the base and microfluidic channels that supply fluid to the domains. 77,

As previously noted, a required element of a *prima facie* case of obviousness is that the prior art references either teach or suggest all of the claim limitations. See also M.P.E.P. § 2143.03 (citing *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974)). As demonstrated above, the Patent Office cannot establish this element of the *prima facie* case. Additionally, the Office cannot establish the first element of the *prima facie* case, a suggestion or motivation to combine, since, as discussed above, Cherukuri and Sanadi describe entirely different devices: a microfluidic device for combinatorial chemistry and a general-purpose multi-well plate, respectively. Since Sanadi is unrelated to the field of microfluidics, one of skill in the art would not be motivated to combine the Sanadi and Cherukuri references. Similarly, the Office cannot establish the second element of the *prima facie* case, a reasonable expectation of success since one skilled in the art could not possibly arrive at the cassette of the present invention by combining the teachings of Cherukuri and Sanadi. Accordingly, we respectfully submit that the Office cannot establish a *prima facie* case that claim 1, as amended, is obvious over the cited references.

b. The Claims Depending From Claim 1 Are Not *Prima Facie* Obvious

While it is fundamental that “If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious,” M.P.E.P. § 2143.03 (citing *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988), the converse is not true. Moreover, under *Graham v. John Deere*, the Patent Office is required to ascertain the differences between the prior art and the claims at issue. Therefore, the Office must separately analyze each claim for patentability under § 103 and ascertain the differences between each claim and the prior art. However, in the Office Action mailed June 4, 2002, the Office analyzed only claim 1, rejecting it under 35 U.S.C. § 103(a). On this ground alone, the Patent Office has failed to establish a *prima facie* case that those claims depending from claim 1 are obvious.

Furthermore, the Patent Office cannot establish a *prima facie* case of obviousness with respect to the claims depending from claim 1—not only because claim 1 itself is nonobvious in view of the cited art (as discussed in the previous section), but also because the dependent claims contain further limitations that are not taught or suggested by the cited prior art. For example, claim 11, as amended, is directed to “The cassette of claim 1, wherein each individual microfluidic channel supplies fluid to a single domain, to provide separate fluid flow to each domain.” In contrast, Cherukuri discloses a cassette wherein “channels and reservoirs form a grid delivery system where reservoirs are grouped into column reservoirs, row reservoirs and matrix reservoirs. . . . The matrix reservoirs are capable of providing reagent fluids to all reaction cells.” See column 3, lines 11-13 and column 7, lines 35-36. Cherukuri’s cassette is designed this way because it is “adapted for performing the processes of combinatorial chemistry,” rather than cell screening. See column 4, lines 41-42. Meanwhile, Sanadi teaches only a multi-well plate containing no microfluidic channels whatsoever, and therefore does not cure the deficiency of Cherukuri.

*Claim 11?*

Based on the above, none of the currently pending claims depending from claim 1 are obvious in light of the cited prior art, since they all recite limitations that are not taught or suggested by the combination of Cherukuri and Sanadi. Therefore, the Patent Office cannot establish a *prima facie* case of obviousness with respect to any of these claims.

c. Claim 17 is Not *Prima Facie* Obvious



As with the claims depending from claim 1, the Office has failed to establish a *prima facie* case of obviousness with respect to claim 17 simply on the ground that the Office has not analyzed the patentability of claim 17. Furthermore, the Office cannot establish a *prima facie* case with respect to claim 17 because it contains limitations that are not taught or suggested by the cited prior art. Claim 17 is directed to the following:

A cassette for cell screening, comprising:

- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites for interaction with different cell types, and wherein the cell binding sites comprise wells, wherein the wells in total comprise cell binding sites for more than one cell type;
- (b) a controlled array of cell types on the wells, wherein the cell type on an individual well is dependent upon the cell binding specificity of the cell binding sites in the well; and
- (c) a fluid delivery system for delivering a combinatorial of reagents to the controlled array of cell types, wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:
  - (i) a plurality of domains matching the wells on the surface of the base; and
  - (ii) microfluidic channels that supply fluid to the domains.

The combination of Cherukuri and Sanadi fail to teach, suggest, or motivate at least the following limitations of claim 17:

- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites for interaction with different cell types, and wherein the cell binding sites comprise wells, wherein the wells in total comprise cell binding sites for more than one cell type;

- (b) a controlled array of cell types on the wells, wherein the cell type on an individual well is dependent upon the cell binding specificity of the cell binding sites in the well;  
and
- (c) a fluid delivery system for delivering a combinatorial of reagents to the controlled array of cell types, wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:
  - (i) a plurality of domains matching the wells on the surface of the base; and
  - (ii) microfluidic channels that supply fluid to the domains.

As previously noted, a required element of a *prima facie* case of obviousness is that the prior art references either teach or suggest all of the claim limitations. See also M.P.E.P. § 2143.03 (citing *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974)). As demonstrated above, the Patent Office cannot establish this element of the *prima facie* case, since the cassette of claim 17 is not taught or suggested by the combination of the cited prior art. Additionally, the Office cannot establish the first element of the *prima facie* case, a suggestion or motivation to combine, since, as discussed above, Cherukuri and Sanadi describe entirely different devices: a microfluidic device for combinatorial chemistry and a general-purpose multi-well plate, respectively. Since Sanadi is unrelated to the field of microfluidics, one of skill in the art would not be motivated to combine the Sanadi and Cherukuri references. Similarly, the Office cannot establish the second element of the *prima facie* case, a reasonable expectation of success since one skilled in the art could not possibly arrive at the cassette of claim 17 by combining the teachings of Cherukuri and Sanadi. Accordingly, we respectfully submit that the Office cannot establish a *prima facie* case that claim 17, as amended, is obvious.

d. The Claims Depending From Claim 17 Are Not *Prima Facie* Obvious

As with the claims depending from claim 1 and as with claim 17, the Office has failed to establish a *prima facie* case of obviousness with respect to the claims depending from claim 17 simply on the ground that the Office has not analyzed the patentability of the claims depending



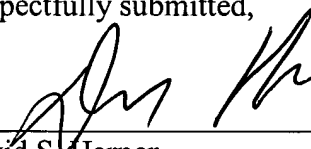
from claim 17. Furthermore, the claims depending from claim 17 are similar to those depending from claim 1. Therefore, like the claims depending from claim 1, the Patent Office cannot establish a *prima facie* case of obviousness with respect to the claims depending from claim 17—both because the cited prior art does not teach or suggest the limitations of claim 17 and also because the dependent claims contain further claim limitations. For example, claim 20 is directed to the cassette of claim 17, “wherein each individual microfluidic channel supplies fluid to a single domain, . . .” a limitation also recited in claim 11.

Based on the above, none of the currently pending claims depending from claim 17 are obvious in light of the cited art, since they all recite limitations that are not taught, suggested, or motivated by the combination of Cherukuri and Sanadi. Therefore, the Patent Office cannot establish a *prima facie* case of obviousness with respect to any of these claims.

3. Conclusion

In view of the remarks above, the application is considered to be in good and proper form for allowance. Therefore, the Patent Office is respectfully requested to pass the application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of this application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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David S. Harper  
Reg. No. 42,636

Dated: December 4, 2002

**Appendix A: Clean Version of the Pending Claims**

- C1
1. (Twice Amended) A cassette for cell screening, comprising
- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites, and wherein a cell binding site comprise a well; and
  - (b) a fluid delivery system for delivering a combinatorial of reagents to the wells; wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:
    - (i) a plurality of domains matching the wells on the surface of the base; and
    - (ii) microfluidic channels that supply fluid to the domains.

9. The cassette of claim 1, wherein the domains are selected from the group consisting of etched domains and raised reservoirs.

10. The cassette of claim 1, wherein the chamber further comprises microfluidic channels that remove excess fluid from the domains.

C2 4 11. (Amended) The cassette of claim 1, wherein each individual microfluidic channel supplies fluid to a single domain, to provide separate fluid flow to each domain.

12. The cassette of claim 1, further comprising a plug between the end of the microfluidic channel and the domains.

13. The cassette of claim 1, wherein a microfluidic channel extends from each domain to an edge of the chamber.

14. The cassette of claim 1, further comprising an array of cells on the wells.

15. The cassette of claim 1, wherein the wells in total comprise cell binding sites for more than one cell type.

16. The cassette of claim 15, further comprising a controlled array of cell types on the wells, wherein the cell type on an individual well is dependent upon the cell binding specificity of the cell binding sites in the well.

10X C4 A cassette for cell screening, comprising:

- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites for interaction with different cell types, and wherein the cell binding sites comprise wells, wherein the wells in total comprise cell binding sites for more than one cell type;
- (b) a controlled array of cell types on the wells, wherein the cell type on an individual well is dependent upon the cell binding specificity of the cell binding sites in the well; and

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concl.  
(c) a fluid delivery system for delivering a combinatorial of reagents to the controlled array of cell types, wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:

- (i) a plurality of domains matching the wells on the surface of the base; and
  - (ii) microfluidic channels that supply fluid to the domains.
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18. The cassette of claim 17, wherein the domains are selected from the group consisting of etched domains and raised reservoirs.

19. The cassette of claim 17, wherein the chamber further comprises microfluidic channels that remove excess fluid from the domains.

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C3 13 20. (Amended) The cassette of claim <sup>10</sup>17, wherein each individual microfluidic channel supplies fluid to a single domain, to provide separate fluid flow to each domain.

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21. The cassette of claim 17, further comprising a plug between the end of the microfluidic channel and the domains.

22. The cassette of claim 17, wherein a microfluidic channel extends from each domain to an edge of the chamber.

**Appendix B: Rewritten Claims With Markings to Show Changes Made**

1. (Twice Amended) A cassette for cell screening, comprising
- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites, and wherein ~~[the]~~ a cell binding site[s] comprise a well[s]; and
  - (b) a fluid delivery system for delivering a combinatorial of reagents to the wells; wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:
    - (i) a plurality of domains matching the wells on the surface of the base; and
    - (ii) microfluidic channels that supply fluid to the domains.
11. (Amended) The cassette of claim 1, wherein ~~[the microfluidic channels match the chamber's domains]~~ each individual microfluidic channel supplies fluid to a single domain, to provide separate fluid flow to each domain~~[-and wherein the domains are larger in diameter than the wells on the surface of the base]~~.
17. (Amended) A cassette for cell screening, comprising:
- (a) a base having a surface, wherein the surface contains a non-uniform micro-patterned chemical array comprising multiple cell binding sites for interaction with different cell types, and wherein the cell binding sites comprise wells, wherein the wells in total comprise cell binding sites for more than one cell type;
  - (b) a controlled array of cell types on the wells, wherein the cell type on an individual well is dependent upon the cell binding specificity of the cell binding sites in the well; and
  - (c) a fluid delivery system for delivering a combinatorial of reagents to the controlled array of cell types, wherein said fluid delivery system comprises a chamber that mates with the base, wherein the chamber comprises:
    - (i) a plurality of domains matching the wells on the surface of the base; and
    - (ii) microfluidic channels that supply fluid to the domains.
20. (Amended) The cassette of claim 17, wherein ~~[the microfluidic channels match the chamber's domains]~~ each individual microfluidic channel supplies fluid to a single domain, to provide separate fluid flow to each domain~~[-and wherein the domains are larger in diameter than the wells on the surface of the base]~~.